What’s New in Pediatric Dermatology?

Frank Morocco D.O. FAOCD
Objectives

- New pathogenesis and treatment of atopic dermatitis
- Allergic contact dermatitis
- Infantile Hemangiomas
- Aquagenic wrinkling of the palms
- Acne and oral isotretinoin
- New treatment options for common diseases
Atopic Dermatitis

The Itch that Rashes
Atopic Dermatitis

- Epithelial barrier disruption
- 50% of atopic dermatitis caused by Filaggrin gene (FLG) disorder
- FLG encodes profilaggrin which is the major component of granular layer.
- Filaggrin makes up the major scaffolding that forms the lipid cell envelope.
Atopic Dermatitis

Diagram Key:
- D: Dendritic cell
- T_0: Naive T cell
- T_{m,1}: Type 1 helper cell
- T_{m,2}: Type 2 helper cell
- B: B cell
- E: Eosinophil
- H_2O: Water
- M: Mast cell
- Ba: Basophil
- MP: Macrophage

Genetic abnormality

Initial

Defective skin barrier

Allergens, Pathogens

Ongoing

Increased cytokines (IL-1, TNF-)

Inflammation

T_{m,1}, MP

Decreased ceramide, filaggrin and antimicrobial peptides

Further damage to the skin barrier

B

pruritus

Inflammation

T_0

Type 2 helper cell

D

Naive T cell
Normal Epidermis
Atopic Dermatitis
Filaggrin

- Filaggrin is degraded and forms “natural moisturizing factor”
- Decreases pH which helps inhibit *Staphylococcus aureus* growth
- Activate enzymes in ceramide metabolism
- Modulating the activity of serine proteases
- Epidermal barrier repair is aimed at replacing ceramides, inhibition of elevated protease activity and decreasing skin pH
Atopic Dermatitis

- In vitro studies have shown immunity still has major effect.
- IL-22 and IL-25 are involved in decreasing filaggrin expression.
- Decrease of active copies of fillagran by 5–10% can increase severity of atopic dermatitis.
Atopic Dermatitis

- **Other Factors**
  - Delayed introduction of solid foods, early life exposure to antibiotics, exposure to farm animals or ingestion of fish oils have no effect on development of AD
  - Breast-feeding has been shown to have no effect
    - Physiologic and psychological benefits of breast feeding makes it preferred feeding modality even in children with risk of developing AD
Children < 5 y/o with Moderate to severe AD should be considered for food allegies to milk, egg, peanut wheat, and soy **IF** persistant atopic dermatitis with optimal treatment or if there is a history of immediate reaction after the ingestion of a specific food.

- Individuals without documented or proven food allergies should **not** avoid potential allergenic foods.
- Fifty percent to 90% of presumed allergies are not allergic in nature.
- Solid foods should not be delayed beyond 4 to 6 months, because this may paradoxically increase the incidence of food allergies.
AD and ADHD

 Proposed Mechanisms
  ◦ Negative effect of inflammatory cytokines on central nervous system
  ◦ Increased stress and sleep disturbances due to pruritis.
  ◦ Lack of impulse control and use of stimulatory medication makes ADHD a risk factor for more severe AD
Atopic Dermatitis

- Increased risk of *S. Aureus* infection and colonization which leads to inflammation
  - Decreased Human Beta-defensin-2 leads to increased MSSA.
- A recent study showed that diluted bleach baths plus intranasal mupirocin led to significant improvement in eczema severity scores.
  - Typical recipe is ¼ cup of bleach for ½ tub of water and ½ cup of bleach for tub full of water
  - Mupirocin was administered 5 consecutive days a month
Atopic Dermatitis

- Wet dressing therapy was has been used in past for severe AD.
- Recent study from Mayo Clinic described their institution’s wet dressing therapy for inpatient hospitalizations.
- 45% had 75%-100% clearance
- 38% had 50%-75% clearance
Atopic dermatitis

- Traditional AD management dogma consisted of application of anti-inflammatory medication to areas of “active” disease.
- Recent research shows a paradigm shift.
- After twice daily active treatment of AD flare, patients were given “proactive” twice weekly treatment with topical tacrolimus and had significant fewer AD flares.
Allergic contact dermatitis

- Pediatric rate of allergic contact dermatitis is increasing and is comparable to adult rates
- Most common relevant contact allergens in children are:
  - Nickel, cobalt, fragrance mix, wool alcohols, thimerosal, neomycin and gold
Car Seat Dermatitis

The shiny “nylon” type of material.

Lower lateral aspects of the elbows and legs. Occipital scalp and posterior thighs.
ACD

- Neoprene dermatitis
- P-tert-butylphenol formaldehyde resin
- Wet suits
- Sport braces
- Mouse pads
- Shin guards
Infantile Hemangiomas

- Infantile hemangiomas are the most common tumor of infancy and arise in 5% to 10% of infants
- Glucose 1 transporter (GLUT-1) has been shown to be specific for infantile hemangiomas
Infantile Hemangiomas with Minimal or Abortive Growth (IH–MAGs)

◦ A recent study observed vascular malformations that had minimal to no growth and were present at birth
◦ Located on lower extremities, buttocks and groin
◦ Found these to be Glucose transporter 1–positive
◦ Pathogenesis may lead us to another pathway for treatment of vascular tumors
Infantile Hemangiomas

- The expected proliferation phase of hemangiomas is during the first year of life with rapid growth until 6–9 months of age.
  - A recent found most rapid growth between age 5.5 – 7.5 weeks
  - Best age for referral 4 weeks old
  - Hemangioma precursors were present at birth in 65% of patients
Infantile hemangiomas

- Early white discoloration heralds impending ulceration
- Usually seen before 3 months of age
- In contrast to the whitish gray color of involution seen several months later
<table>
<thead>
<tr>
<th>LUMBAR</th>
<th>PHACE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lower body segmental IH</strong></td>
<td>Posterior fossa malformation</td>
</tr>
<tr>
<td><strong>Urogenital anomalies and Ulceration</strong></td>
<td>*Hemangioma (facial)</td>
</tr>
<tr>
<td><strong>Myelopathy (most common)</strong></td>
<td>Arterial anomalies</td>
</tr>
<tr>
<td><strong>Bony deformities</strong></td>
<td>Cardiac defects</td>
</tr>
<tr>
<td><strong>Anorectal malformations and Arterial anomalies</strong></td>
<td>Eye anomalies</td>
</tr>
<tr>
<td><strong>Renal anomalies</strong></td>
<td>*Lower GI segmental hemangiomas</td>
</tr>
<tr>
<td></td>
<td>Magnetic Resonance Angiography is best diagnostic test</td>
</tr>
</tbody>
</table>
One of the greatest breakthroughs in pediatric dermatology has revolved around IH and propranolol.

Mechanism of action is unknown

- Vasocostriction
- Blocking proangiogenic signals
- Apoptosis of endothelial cells
Infantile Hemangioma

- **2008**– The discovery was made after 2 children with cardiac issues were treated with oral beta blockers with great effectiveness.

- **2009**– 32 children treated with oral propranolol all had good response.
**Infantile Hemangioma**

- 2011 – 40 pts given 2 mg/kg per day divided 3 times daily for 6 months.
- Baseline electrocardiogram, echocardiogram, and laboratory evaluations were performed. Monitoring of heart rate, blood pressure, and blood glucose was performed at each visit.
- No significant hypoglycemia, hypotension, or bradycardia occurred.
- Growth stopped at 4 weeks
Infantile hemangiomas

- 2011 – Propranolol vs corticosteroids
  - multicenter retrospective analysis
  - 139 patients
  - 82% achieved clearance of 75% or more on propranolol compared to 29% who were receiving oral corticosteroids
  - This study helped show superior efficacy with fewer side effects.
Infantile Hemangiomas that ulcerate are prone to considerable morbidity with pain, infection, and scarring. Challenging to treat. When compared to traditional modalities for treatment (PDL, wound care, oral antibiotics and oral corticosteroids) propranolol was found to shorten time to healing after the onset of ulceration. Average time to heal from onset of ulceration with propranolol 8.7 weeks compared to 22.4 weeks with wound care. Head and neck hemangiomas 4.3 weeks to heal and 14.5 days to achieve pain control.
Propranolol is now considered standard of care for severe IH but it is being used more in less aggressive IH.

Most patients are started on a low dose and titrated up to 2 mg/kg/day in divided doses.

Rare side effects include hypoglycemia, hypotension, and exacerbation of asthma.

More common side effects are cold extremities and night terrors.
Other systemic beta blocker are being examined. Atenolol is a hydrophilic beta–1 antagonist that may decrease pulmonary side effects and sleep disturbances. Nadolol has been compared to propranolol in a small case study which showed superior efficacy decreased side effects and easier dosing schedules due to a longer half life. Topical beta–blocker in the form of timolol has been tried with success for superficial small hemangiomas not requiring systemic treatment
Aquagenic Wrinkling of Palms
Aquagenic Wrinkling of Palms

- Aquagenic Wrinkling of palms found in cystic fibrosis and carrier state.
- Studies show AWP in 41% to 84% of patients with CF
- Most individuals 11.5 minutes
- CF develop changes within 2 minutes
- Carries within 7 minutes
- All pts with AWP should have complete ROS and PE looking for: chronic fatigue, sinus drainage, nasal polyps, wheezing, reactive airway disease, abdominal disease and clubbing.
Biologics in pediatric population

- An explosion of biologic medicine is available for adults with psoriasis.
- The FDA has not approved these for the use of children.
- 2008 multicenter, double blind, placebo controlled trial showed etanercept to be effective for as young as 4 years of age.
- 2010 – Intermittent and long term exposure of entanercept for 2 years showed sustained improvement.
Oral Isotretinoin and Mood

- 2% of adolescents 13 – 17 years of age will have a major depressive episode unrelated to medication
- Suicidal ideations in boys with acne 3 times more common than boys without acne
- Several recent studies have shown either no change or improvement in mood during or after treatment with oral isotretinoin
Oral isotretinoin

- A recent retrospective review did report dose dependent mood changes in 7.1% of patients taking isotretinoin.
- In another report 9 out of 10 patients with bipolar disease had significant worsening of mood and 8 of the 9 had reversal in symptoms with discontinuation with therapy.
Oral Isotretinoin and IBD

- 1985 – the first case of IBD was reported in a patient on oral isotretinoin there have been several case reports that showed a vague connection
- 2009– an appraisal of the literature and a case controlled study indicated no correlation.
Oral Isotretinoin and IBD

- 2010 – large case control study showed an odds ratio of 4.36 for ulcerative colitis and isotretinoin at any level, but no increased association with Crohn’s disease
- Tetracycline antibiotics, especially doxycycline, have been linked to increased risk of IBD
- What is Cause?
Tinea Capitis

- Treatment with oral griseofulvin 20 to 25 mg/kg/day with adjunctive selinium sulfide 2.5% for 6 weeks shows moderate success.
- Most common dermaytophyte of scalp is *Trichophyton tonsurans*
- Several randomized studies have shown oral terbinifine (dosing ranging from 3 to 8 mg/kg /day for duration of 2–4 weeks) have faster and superior cure rates for *Trichophyton tonsurans*
References

References


References


